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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/712,985	11/13/2003	Franciscus Petrus Nijkamp	92750/66	7336

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EXAMINER	
RUSSEL, JEFFREY E	

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 01/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/712,985	NIJKAMP ET AL.	
	Examiner	Art Unit	
	Jeffrey E. Russel	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 22-32 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 22-32 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 November 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/958,049.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20031113*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. The disclosure is objected to because of the following informalities: At page 6, between lines 27 and 28, the heading "Brief Description of the Drawings" should be inserted. Page 13, line 5, of the specification refers to a "Fig. 3". However, only two figures have been filed with the application. It is believed that the specification should have referred to "Fig. 2". Appropriate correction is required.

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 22-24, 26, 27, and 29-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. There is no original disclosure of peptides having sequences complementary to proline-glycine-proline, as is recited in independent claims 22, 26, and 29. There is no literal support in the original disclosure for this new claim terminology. The concept of a "complementary" sequence is also not present in the original disclosure of the invention. Compare, e.g., page 2, lines 7-12, where there is disclosure of peptides which bind to and complex with PGP-comprising compounds. However, binding and complexing are different chemical actions than complimentary-ness (see also the rejection under 35 U.S.C. 112, second paragraph, set forth below). Applicants cite to page 1, lines 2-15, as support for the new claim language. However, this section of the specification does not discuss the concept of "complementary" peptides. The preliminary amendment in which new claims 22-24, 26, 27, and

29-31 occur does not constitute part of the original disclosure of the invention because the preliminary amendment was not referred to in the declaration filed on the same date as this application. See MPEP 608.04(b) and 714.01(e)(II). There is no original disclosure of the treatment of acute respiratory distress syndrome (ARDS) as is recited in instant claims 29-31. Note that the original disclosure defines "ARDS" as adult respiratory distress syndrome. See, e.g., page 6, lines 26-27, of the specification.

4. Claims 22-24, 26, 27, and 29-31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are drawn to methods of treating autoimmune diseases, heart disease characterized by an influx of neutrophilic granulocytes, and acute respiratory distress syndrome where the active agents are defined functionally and only partially by structure (the active agents are required to be peptides). The claims could literally embrace an uncountable number of peptides. However, only one specific example of such an active agent is described in the specification, i.e. the peptide comprising the sequence arginine-threonine-arginine. Note that 4-RTR merely comprises multiple copies of the same arginine-threonine-arginine sequence. The specification does not provide any guidance, theoretical basis for predicting, or method of obtaining compounds which might satisfy the claimed functional requirements, nor does the specification provide any guidance or theoretical basis for identifying compounds which would be able to treat the disorders recited in the claims. This would result in the necessity of random trial and error of all available chemicals. The limited number of specific examples do not

demonstrate that Applicants had possession of the entire genus of claimed compounds for all of the claimed uses, and therefore Applicants can not be said to have provided an adequate written description of the claimed invention.

5. Claims 22-24, 26, 27, and 29-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Independent claims 22, 26, and 29 recite the use of a peptide which has a sequence which is "complementary" to proline-glycine-proline. It is not clear what constitutes a "complementary" sequence as claimed by Applicants. It is not clear if the term refers to some spatial or charge relationship between the peptides and the PGP. It is not clear if the term requires the peptide to bind to the PGP (one skilled in the art could imagine a peptide which is spatially complementary to PGP but which would not bind to or complex with PGP due to charge or lipophilic/hydrophilic repulsions), and if so, it is not clear if the term requires the peptide to neutralize some property or function of PGP. The term is not defined either in the specification or the art.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

For the purposes of this invention, the level of ordinary skill in the art is deemed to be at least that level of skill demonstrated by the patents in the relevant art. Joy Technologies Inc. v. Quigg, 14 USPQ2d 1432 (DC DC 1990). One of ordinary skill in the art is held accountable not only for specific teachings of references, but also for inferences which those skilled in the art may reasonably be expected to draw. In re Hoeschele, 160 USPQ 809, 811 (CCPA 1969). In addition, one of ordinary skill in the art is motivated by economics to depart from the prior art to reduce costs consistent with desired product properties. In re Clinton, 188 USPQ 365, 367 (CCPA 1976); In re Thompson, 192 USPQ 275, 277 (CCPA 1976).

7. Claims 22 and 25 are rejected under 35 U.S.C. 102(a) and (e) as being anticipated by Tuomanen et al (U.S. Patent No. 5,932,217). Tuomanen et al teach the peptide GRTRG (SEQ ID NO:8), which is used in pharmaceutical compositions to inhibit adhesion between leukocytes and endothelial cells and to inhibit the influx of leukocytes into inflamed tissue, and to control inflammation in autoimmune diseases. See, column 13, lines 14-16, and claims 1 and 5. The claimed peptide of Tuomanen et al comprises RTR. In view of the similarity in structure and function between the claimed peptide of Tuomanen et al and Applicants' claimed peptides, inherently the claimed peptide of Tuomanen et al will have a sequence complementary to PGP to

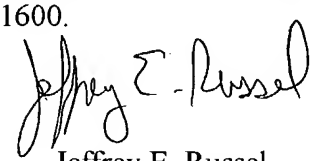
the same extent claimed by Applicants. Sufficient evidence of similarity is deemed to be present between the method of Tuomanen et al and Applicants' claimed method to shift the burden to Applicants to provide evidence that the claimed method is unobviously different than that of Tuomanen et al.

8. Claims 23, 24, 26-30, and 32 are rejected under 35 U.S.C. 103(a) as being obvious over Tuomanen et al (U.S. Patent No. 5,932,217) as applied against claims 22 and 25 above, and further in view of Ringler et al (U.S. Patent Application Publication 2002/0172679), Harlan et al (U.S. Patent Application Publication 2001/0006656), Morin, Jr. et al (U.S. Patent No. 6,013,674), or Thorsett et al (U.S. Patent No. 6,489,300. Tuomanen et al teach pharmaceutical compositions capable of inhibiting adhesion between leukocytes and endothelial cells, inhibiting the influx of leukocytes into inflamed tissue, and controlling inflammation in autoimmune diseases, but do not teach the use of these compositions to treat inflammatory bowel disease, rheumatoid arthritis, heart ischemia, or ARDS such as asthma. Ringler et al teach treating inflammatory bowel disease by inhibiting the binding of leukocytes to gut-associated endothelium. See, e.g., the Abstract. Harlan et al teach that blockade of leukocyte or endothelial adhesion molecules has been demonstrated to be of benefit in models of chronic inflammatory-immune diseases, such as asthma, arthritis, and inflammatory bowel disease. See, e.g., paragraph [0046]. Morin, Jr. et al teach inhibiting leukocyte adhesion to endothelial cells so as to treat inflammatory diseases and other conditions, such as rheumatoid arthritis, asthma, respiratory distress syndrome, ischemia, and inflammatory bowel disease. See, e.g., the Abstract and column 1, line 64 - column 2, line 3. Thorsett et al teach that leukocyte migration after myocardial ischemia causes further injury to the tissue, and teaches administering inhibitors of

leukocyte adhesion in order to prevent such injury, and in order to treat other leukocyte-mediated conditions such as inflammatory bowel disease, rheumatoid arthritis, asthma, and ARDS. See, e.g., the Abstract; column 2, lines 47-50; and column 22, lines 48-59. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to use the pharmaceutical compositions of Tuomanen et al to treat inflammatory bowel disease, rheumatoid arthritis, heart ischemia, ARDS, and asthma, because it is desirable in the art to treat these diseases, because Ringler et al, Harlan et al, Morin, Jr. et al, and/or Thorsett et al teach that these diseases can be treated by inhibiting leukocytes migration and/or adhesion, e.g., to endothelial tissues, and because Tuomanen et al teach that their pharmaceutical compositions have the function which is taught by Ringler et al, Harlan et al, Morin, Jr. et al, and Thorsett et al to be useful in treating these diseases.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (571) 272-0969. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Bruce Campell can be reached at (571) 272-0974. The fax number for formal communications to be entered into the record is (571) 273-8300; for informal communications such as proposed amendments, the fax number (571) 273-0969 can be used. The telephone number for the Technology Center 1600 receptionist is (571) 272-1600.



Jeffrey E. Russel
Primary Patent Examiner
Art Unit 1654

JRussel
December 28, 2004